

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Andrew C. CHAN et al.

Application No.: 10/538,125

Confirmation No.: 2225

Filing Date (Int'l): December 11, 2003

Art Unit: 1633

For: TRANSGENIC MICE EXPRESSING HUMAN
CD20

Examiner: Q. Li

AMENDMENT IN RESPONSE TO NON-FINAL OFFICE ACTION

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

INTRODUCTORY COMMENTS

This is in response to the non-final Office Action dated June 6, 2007, for which a response was due on September 6, 2007. Filed herewith is a Petition and fee for a two-month extension of time, thereby extending the deadline for response to November 6, 2007. Accordingly, this response is timely filed. Reconsideration and allowance of the pending claims, as amended, in light of the remarks presented herein are respectfully requested.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 6 of this paper.

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Claim 1 (currently amended): A ~~non-human~~ transgenic mouse ~~animal~~ whose genome comprises a nucleotide sequence encoding human CD20.

Claim 2 (currently amended): The transgenic mouse ~~animal~~ of claim 1 wherein said nucleotide sequence is operably linked to a human endogenous promoter.

Claim 3 (currently amended): The transgenic mouse ~~animal~~ of claim 2 whose cells express human CD20.

Claim 4 (currently amended): The transgenic mouse ~~animal~~ of claim 3 wherein human CD20 is expressed on the surface of B lymphocytes.

Claim 5 (currently amended): The transgenic mouse ~~animal~~ of claim 3 wherein human CD20 is expressed on the B lymphocytes at a level sufficient for anti-human CD20 antibody bound to the expressing cells to affect killing of the cells, resulting in B cell depletion.

Claim 6 (currently amended): The transgenic mouse ~~animal~~ of claim 1 wherein the genome of said mouse ~~animal~~ contains a disruption in an endogenous gene encoding a CD20 molecule substantially homologous to human CD20.

Claim 7 (currently amended): The transgenic mouse ~~animal~~ of claim 6, wherein the endogenous gene encodes a murine CD20.

Claim 8 (currently amended): A method of identifying an agent capable of treating a B cell lymphoma said method comprising: a) measuring the number level of B lymphocytes and/or pre-B cells expressing human CD20 in a mouse ~~an animal~~ of claim 1; b) administering said agent to the mouse ~~animal~~ of claim 1; and c) measuring the number level of B lymphocytes and/or pre-B cells expressing human CD20 in the mouse ~~animal~~; wherein a decrease in the number of B lymphocytes

and/or pre-B cells expressing human CD20 in the mouse animal after treatment with the agent identifies the agent capable of treating a B cell lymphoma.

Claim 9 (canceled)

Claim 10 (currently amended): A method of identifying an agent capable of depleting or killing B lymphocytes and/or pre-B cells expressing human CD20 said method comprising: a) measuring the number level of B lymphocytes and/or pre-B cells expressing human CD20 in a mouse an animal of claim 1; b) administering said agent to the mouse animal of claim 1; and c) measuring the number level of B lymphocytes and/or pre-B cells expressing human CD20 in the mouse animal; wherein a decrease in the number of B lymphocytes and/or pre-B cells expressing human CD20 in the mouse animal identifies the agent as capable of depleting or killing B lymphocytes and/or pre-B cells expressing CD20.

Claim 11 (original): The method of claim 10 wherein said cells are cancer cells.

Claim 12 (canceled)

Claim 13 (currently amended): A cell or tissue derived from the transgenic mouse animal of claim 1.

Claim 14 (canceled)

Claim 15 (canceled)

Claim 16 (currently amended): A method of testing safety of anti-human CD20 therapy, said method comprising: a) ~~measuring the level of B lymphocytes expressing human CD20 in an animal of claim 1;~~ b) ~~administering said agent to the animal of claim 1;~~ and c) ~~measuring the level of B lymphocytes expressing human CD20 in the animal;~~ wherein a decrease in the number of B lymphocytes expressing human CD20 in the animal identifies the agent as capable of depleting or killing cells expressing CD20; d) monitoring ~~monitoring a mouse of claim 1 that has been administered an agent capable of depleting or killing B lymphocytes and/or pre-B cells expressing CD20~~ the animal for short or long term adverse effects.

Claim 17 (currently amended): A method of testing efficacy of anti-human CD20 therapy, said method comprising: ~~a) measuring the level of B lymphocytes expressing human CD20 in a set of animals of claim 1; b) administering to each animal of the set a different dose of an agent; and c) measuring the level of B lymphocytes expressing human CD20 in animal after each dose; and d) determining at least one dose of an agent that results in the most B cell depletion in a set of mice of claim 1 that have each been administered a different dose of the agent; wherein the amount of B cell depletion is determined by measuring the number of B lymphocytes and/or pre-B cells expressing human CD20 in the set of mice of claim 1.~~

Claim 18 (new): The transgenic mouse of claim 2 wherein the promoter is a human CD20 promoter.

Claim 19 (new): The transgenic mouse of claim 1 wherein said nucleotide sequence is operably linked to a murine CD20 promoter.

Claim 20 (new): The method of claim 8 wherein the number of B lymphocytes is measured.

Claim 21 (new): The method of claim 10 wherein the number of B lymphocytes is measured.

Claim 22 (new): The method of claim 16 wherein the agent decreases the number of B lymphocytes.

Claim 23 (new): The method of claim 17 wherein the number of B lymphocytes is measured.

Claim 24 (new): A method of identifying an agent capable of treating a B cell lymphoma said method comprising comparing the number of B lymphocytes and/or pre-B cells expressing human CD20 in a mouse of claim 1 after administering an agent to the mouse to the number of B lymphocytes and/or pre-B cells expressing human CD20 in the mouse before administration of the agent, wherein a decrease in the number of B lymphocytes and/or pre-B cells expression human CD20 in the mouse after administration of the agent compared to the number of B lymphocytes

and/or pre-B cells expressing human CD20 in the mouse before administration of the agent identifies the agent capable of treating a B cell lymphoma.

Claim 25 (new): The method of claim 24 wherein the number of B lymphocytes is measured.

Claim 26 (new): A method of identifying an agent capable of depleting or killing B lymphocytes and/or pre-B cells expressing human CD20 said method comprising comparing the number of B lymphocytes and/or pre-B cells expressing human CD20 in a mouse of claim 1 after administering an agent to the mouse to the number of B lymphocytes and/or pre-B cells expressing human CD20 in the mouse before administration of the agent, wherein a decrease in the number of B lymphocytes and/or pre-B cells expression human CD20 in the mouse after administration of the agent compared to the number of B lymphocytes and/or pre-B cells expressing human CD20 in the mouse before administration of the agent identifies the agent capable of depleting or killing B lymphocytes and/or pre-B cells expressing CD20.

Claim 27 (new): The method of claim 26 wherein said cells are cancer cells.

Claim 28 (new): The method of claim 26 wherein the number of B lymphocytes is measured.

REMARKS

Claims 1-17 were pending in the present application prior to this amendment. Claims 18-28 have been added, claims 1-8, 10, 13, 16, and 17 are amended, and claims 9, 12, 14, and 15 are canceled. Thus, claims 1-8, 10, 11, 13, 16-28 are pending in the application after the entry of this amendment. Support for amended claims 1-8, 10, 13, 16, and 17 is provided throughout the specification, such as at page 24, lines 10-31; page 34, lines 14-16; Examples 1-3; and original claim 15. Support for new claim 18 is provided throughout the specification, such as at page 10, lines 1-14. Support for new claim 19 is provided throughout the specification, such as at page 23, lines 9-27. Support for new claims 24 and 26 is provided throughout the specification, such as at page 3, lines 6-14; and pages 26 and 27. Support for new claims 20-23, 25, and 28 is provided throughout the specification, such as at pages 26 and 27. Support for new claim 27 is provided, for example, in original claim 11. Accordingly, no new matter has been added.

With respect to all claim amendments and cancellations, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in a future continuation and/or divisional application.

Telephone Interview with Examiners

Applicants thank Examiner Janice Li and Examiner Joseph Weitach for extending the courtesy for a telephone interview on October 23, 2007, with Applicants' representative Jie Zhou, and for providing helpful suggestions which are reflected in this response. Pending claims and the rejections in the Office Action were discussed and suggested amendments are reflected in this response. No specific reference was discussed.

Information Disclosure Statements

Applicants thank the Examiner for having considered the references previously submitted in the Information Disclosure Statements.

Priority Claim

The Examiner states that the disclosures of the priority applications U.S.S.N. 60/434,115 and 60/476,481 fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S. § 112 for one or more claims in the present application. In particular, the Examiner states that no transgenic animal was disclosed. Applicants respectfully traverse.

U.S.S.N. 60/434,115 discloses human CD20 transgenic mice, *e.g.*, at Example 12. U.S.S.N. 60/476,481 also discloses human CD20 transgenic mice, *e.g.*, at Examples 3 and 4 and Figure 14-29. These human CD20 transgenic mice were generated from human CD20 BAC DNA. Therefore, at least one claim (*e.g.*, claim 1) is supported in U.S.S.N. 60/434,115 and 60/476,481. Accordingly, the present application is entitled to claim priority to U.S.S.N. 60/434,115 and 60/476,481.

Applicants respectfully request that the Office acknowledge priority to U.S.S.N. 60/434,115 and 60/476,481.

Claim Rejection Under 35 USC § 102

Claims 9 and 12 are rejected under 35 USC § 102(b) as allegedly being anticipated by Reisner *et al* (U.S. Pat. No. 5,849,288).

In the interest of expediting prosecution, claims 9 and 12 have been canceled. Accordingly, this rejection is now moot. Applicants respectfully request that this rejection be withdrawn.

Claim Rejections Under 35 USC § 112, first paragraph

A. Claims 9 and 12 are rejected under 35 USC § 112, first paragraph, as allegedly failing to comply with the written description and enablement requirements.

As noted above, claims 9 and 12 have been canceled in the interest of expediting prosecution. Accordingly, this rejection is now moot. Applicants respectfully request that this rejection be withdrawn.

B. Claims 1-8, 10, 11, 13, 14, 16, and 17 are rejected under 35 USC § 112, first paragraph, as allegedly non-enabled. The Examiner states that the specification, while being enabling for making and using a transgenic mouse whose genome comprises a homozygous insertion of a nucleic acid encoding human CD20, does not provide enablement for making and using a transgenic animal beyond a mouse.

Applicants respectfully disagree with the Examiner that the specification does not enable the making and using of a transgenic animal beyond a mouse.

However, in the interest of expediting prosecution, claims 1-8, 10, 11, 13, 14, 16, and 17 have been amended to specify that the transgenic animal is a mouse. Additionally, Applicants note that the specification enables the making and using of both heterozygous and homozygous human CD20 transgenic mice (see, for example, page 11, lines 32 and 33). For example, page 31, lines 19-32 and Figure 1 demonstrate that heterozygous human CD20 transgenic mice express human CD20 on their B220+ B cells. Because they express human CD20 on their B cells, heterozygous human CD20 transgenic mice can be used to study the function of human CD20, to identify agents useful for treating and diagnosing CD20-associated human diseases, and to test the efficacy or safety of anti-human CD20 therapies (see, for example, pages 25-31). As taught on page 20, lines 1-3, and page 21, lines 1-3, heterozygous mice can be mated to generate homozygous human CD20 transgenic mice. Accordingly, the specification enables the production and use of both heterozygous and homozygous human CD20 transgenic mice.

Applicants respectfully request that this rejection be withdrawn.

C. Claim 10 is further rejected under 35 USC § 112, first paragraph, because the specification allegedly fails to teach how a test of B lymphocytes relates to any and all cell types. Applicants respectfully traverse.

In the interest of expediting prosecution, claim 10 has been amended to refer to the testing of B lymphocytes and/or pre-B cells expressing human CD20. In particular, Figure 2 indicates that human CD20 is expressed on pre-B cells, immature B cells, and mature B cells in human CD20

transgenic mice (see, for example, page 34, lines 14-16). Thus, human CD20 transgenic mice can be used to identify an agent capable of depleting or killing B lymphocytes and/or pre-B cells expressing human CD20.

Applicants respectfully request that this rejection be withdrawn.

Claim Rejection Under 35 USC § 112, second paragraph

Claims 8-12, 16, and 17 are rejected under 35 USC § 112, second paragraph, as allegedly being indefinite because of the recitation of “the level of B lymphocytes.” Applicants respectfully traverse. This term’s meaning is understood by one skilled in the art.

In the interest of expediting prosecution, Applicants have amended claims 8, 10 (from which claim 11 depends), 16, and 17 to specify that the “number” of B lymphocytes and/or pre-B cells is measured. Claims 9 and 12 have been canceled.

Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 146392000401. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: November 6, 2007

Respectfully submitted,

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